Claims

1. A composition comprising a polypeptide comprising at least two antigen binding sites, wherein said at least two antigen binding sites are located on a single polypeptide chain, and wherein
   - one of said at least two antigen binding sites specifically binds the human CD3 antigen;
   - said polypeptide may exist in both monomeric form and multimeric form, said monomeric form being said single polypeptide chain and said multimeric form comprising at least two of said single polypeptide chains non-covalently associated with one another; and
   - said multimeric form of said polypeptide constitutes no more than 5% of the total weight of the combined monomeric and multimeric forms of said polypeptide.

2. The composition of claim 1, wherein at least one of the two antigen binding sites comprises a variable region from the heavy chain of an antibody (VH) and a variable region from the light chain of an antibody (VL).

3. The composition of claim 1 or 2, wherein the other antigen binding site of said at least two antigen binding sites specifically binds to the human CD19 antigen or the human EpCAM antigen.

4. The composition of claim 3, wherein the other antigen binding site of said at least two antigen binding sites specifically binds to the human CD19 antigen and wherein said polypeptide has a sequence as depicted in any of SEQ ID NOs: 1-6 or a sequence which is at least 70% homologous to any of SEQ ID NOs: 1-6.

5. A method of producing a composition of any claims 1-4 in which the amount of a polypeptide in monomeric form has been enriched relative to the amount of said polypeptide in multimeric form, wherein
   - said polypeptide comprises at least two antigen binding sites on a single polypeptide chain, and one of said at least two antigen binding sites specifically binds the human CD3 antigen;
   - said polypeptide in monomeric form is said single polypeptide chain; and

- said polypeptide in multimeric form comprises at least two of said single polypeptide chains non-covalently associated with one another;

said method comprising the following steps:

a) providing the composition comprising said polypeptide in both multimeric and monomeric form;

b) isolating said polypeptide in both multimeric and monomeric form from said composition, said isolating accomplished by

(b1) applying said composition to a first chromatographic material comprising a metal ion;

(b2) removing any components of said composition which have not bound to said first chromatographic material by washing said first chromatographic material with a first buffer; and

(b3) eluting said polypeptide in both multimeric and monomeric form from said first chromatographic material by applying imidazole to said first chromatographic material in a concentration of at least 60 mM;

(b4) collecting a first eluate comprising said polypeptide in multimeric form and said polypeptide in monomeric form;

c) performing a precursor step that is preparatory for the separation of said polypeptide in multimeric form from said polypeptide in monomeric form to occur in step (d), said precursor step accomplished by

(c1) applying said first eluate to a second chromatographic material, which is an ion exchange material;

(c2) removing any components of the first eluate which have not bound to said second chromatographic material by washing said second chromatographic material with a second buffer;

(c3) eluting said polypeptide in multimeric and monomeric form from said second chromatographic material by applying sodium chloride to said second chromatographic material in a concentration of at least 200 mM;

(c4) collecting a second eluate;

d) performing a separation of said polypeptide in multimeric form from said polypeptide in monomeric form, said separation accomplished by

(d1) applying said second eluate to a third chromatographic material allowing separation on the basis of molecular weight;

(d2) translocating components of the applied second eluate along said third chromatographic material by applying a running buffer to said third chromatographic material;

(d3) collecting a third eluate in fractions;

e) analyzing said fractions of said third eluate individually to obtain a measure of the amount of said polypeptide in monomeric form relative to the amount of polypeptide in multimeric form in each fraction; and

f) combining fractions of said third eluate which (almost) exclusively contain the polypeptide in monomeric form to obtain a composition enriched in the polypeptide in the monomeric form.

6. The method of claim 5, wherein steps (b2) and/or (c2) is/are performed by means of chromatography on a column or by means of a batch process, wherein it is preferred that steps (b2) and (c2) are performed on a column.

7. The method of claim 5 or 6, wherein said first chromatographic material comprises the Zn^{2+} or the Ni^{2+} ion.

8. The method of any of claims 5-7, wherein said second chromatographic material allows separation on the basis of anion exchange.

9. The method of any of claims 5-8, wherein said washing of steps b2 and c2 is performed using a volume of first and/or second buffer which is 6 to 10 times greater than the volume of the first and/or second chromatographic material, respectively.

10. The method of any of claims 5-9, wherein said translocating of step d2 is accomplished by applying a volume of said running buffer equivalent to 3 to 7 times the volume of the third chromatographic material.

11. The method of any of claims 5-10, wherein said first and second buffer are each phosphate buffer pH 8.

12. The method of any of claims 5-11, wherein said running buffer in step d2 is selected from phosphate buffer pH 7.0-7.5 and citrate/lysine buffer pH 6.0-7.5.

13. The method of any of claims 5-12, further comprising the step(s) of analyzing the composition enriched in the polypeptide in the monomeric form obtained in step f to

obtain a measure of the amount of said polypeptide in monomeric form relative to the amount of polypeptide in multimeric form in said composition and, optionally, further comprising the step of enriching the content of polypeptide in monomeric form relative to the content of polypeptide in multimeric form by repeating steps d through f on said composition enriched in the polypeptide in the monomeric form.

14. The method of any of claims 5-13, wherein said analyzing is performed using a chromatographic method which separates substances on the basis of their molecular weight.

15. The method of claim 14, wherein said chromatographic method is size exclusion chromatography, in particular high performance size exclusion chromatography.

16. The method of any of claims 5-15, wherein

- said imidazole is applied either as a concentration gradient or as a single concentration and/or
- said sodium chloride is applied either as a concentration gradient or as a single concentration.

17. The method of claim 16, wherein

- said imidazole is applied in a single concentration chosen from the following concentrations: 70 mM, 80 mM, 90 mM, 100 mM, 110 mM and 120 mM; and
- said sodium chloride is applied in a single concentration chosen from the following concentrations: 370 mM, 380 mM, 390 mM, 400 mM, 410 mM and 420 mM.

18. The method of claim 17, wherein said imidazole is applied in a concentration of 80 mM and/or said sodium chloride is applied in a concentration of 400 mM.

19. A composition obtainable by the method of any of claims 5-18.

20. A method for the prevention, treatment or amelioration of a proliferative disease, a minimal residual cancer, a tumorous disease, an inflammatory disease, an immunological disorder, an autoimmune disease, an infectious disease, a viral disease, an allergic reaction, a parasitic reaction, a graft-versus-host disease, a

host-versus-graft disease or a B cell malignancy, the method comprising the step of administering to a subject in need of such a prevention, treatment or amelioration the composition of any of claims 1-5 or claim 19.

21. Use of the composition of any of claims 1-5 or claim 19 for producing a medicament for the prevention, treatment or amelioration of a proliferative disease, of a minimal residual cancer, of a tumorous disease, of an inflammatory disease, of an immunological disorder, of an autoimmune disease, of an infectious disease, of a viral disease, of an allergic reactions, of a parasitic reaction, of a graft-versus-host disease, of a host-versus-graft disease or of a B cell malignancy.

22. The method and use of claim 20 or 21, respectively, wherein prevention, treatment or amelioration of the disease or disorder occurs in a human.

23. The method and use of any of claims 20-22, wherein said tumorous disease is selected from the group consisting of a lymphoma, a B-cell leukemia or a Hodgkin lymphoma.

24. The method and use of any of claims 20-22, wherein said B cell malignancy is a non-Hodgkin lymphoma.

25. The method and use of any of claims 20-22, wherein said autoimmune disease is selected from rheumatoid arthritis, multiple sclerosis, type 1 diabetes mellitus, inflammatory bowel disease, systemic lupus erythematosus, psoriasis, scleroderma and autoimmune thyroid diseases.